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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/062,131	02/01/2002	John C. Russell	6885.US.O1	2508
23492	7590	07/27/2004	<div>EXAMINER</div> <div>CEPERLEY, MARY</div>	
STEVEN F. WEINSTOCK ABBOTT LABORATORIES 100 ABBOTT PARK ROAD DEPT. 377/AP6A ABBOTT PARK, IL 60064-6008			<div>ART UNIT</div> <div>1641</div>	<div>PAPER NUMBER</div>

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/062,131	Applicant(s) RUSSELL, JOHN C.	
	Examiner Mary (Molly) E. Ceperley	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 19, 20, 26 and 27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 19, 20, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>02/01/2002</u> . | 6) <input type="checkbox"/> Other: _____ |

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1) It is noted that references AD and AE of form PTO-1449 filed February 01, 2002 do not appear to be pertinent to the invention described in the instant application.

Reference AL of form PTO-1449 is not present in the file of this application and has not been considered.

2) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

3) The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4) Claims 1, 19, 20, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) In claim 1, it is unclear what is meant by the term "surface-bound protein complex" of step b). It is unclear whether what is intended is a "surface-bound protein" *per se* or whether additional unspecified component(s) are also included in the "complex". This problem also occurs in step d): see the term "stable complex".

b) It is unclear what is meant by the term "second macromolecule" as it is used in claim 1 since there is no requirement for the use of any "first macromolecule". It is also unclear exactly what is meant by the term "macromolecule" since the specification contains examples but no specific definitions of this term; it is unclear what basic chemical structure and functional group(s) are required for the "macromolecule" to be operational for the purposes of the invention.

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c) For claims 19 and 20, there is no antecedent basis in claim 1 for the term "antibody".

Additionally, it is unclear which component of the "conjugate" comprises the "antibody".

d) For claim 19, given the fact that claim 1 recites reacts "a protein" with "the reactive solid-surface" and then further with "a second macromolecule", it is not clear why the designation "only one" is used.

e) For claim 20, it is unclear what is meant to be included by the term "predetermined".

f) For claim 20, given the fact that claim 1 recites reacts "a protein" with "the reactive solid-surface" and then further with "a second macromolecule", the designation "between 2 and 30" is inappropriate.

g) In claim 1, steps a) and b), there is no antecedent basis for the term "the reactive solid-surface".

h) In claim 1, there is no antecedent basis for the term "the protein conjugate" of step d).

i) For claim 1, step c), it is unclear why the "Second Macromolecule" would need to ever be "activated" since step d) requires the use of "a reactive Second Macromolecule".

j) Regarding claim 26, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

l) For claim 26, there is no antecedent basis in claim 1 for the term "first macromolecule". It is also unclear what is meant by the term "one of the macromolecules" since claim 1 recites only one macromolecule, i.e. a "second macromolecule".

m) In claim 26, what is meant by the term "other macromolecules" is unclear since claim 1 refers only to a single "second macromolecule".

n) In claim 26, it is unclear exactly what is encompassed by the terms "the conjugate" and "final conjugate".

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o) In claim 27, it is unclear what is meant by "the macromolecule".

5) The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6) Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Yu et al (U.S. 6,492,105 B2).

Yu et al describe a method of attaching a protein to a functionalized solid surface through a hydrazone linkage to form a solid surface-protein complex as described in steps a) through c) of instant claim 1. See Yu et al: EXAMPLE II, wherein the hydrazide-containing peptides were immobilized to a functionalized solid support via hydrazone bond formation. The solid surface-protein complex of Yu et al is then further contacted with a second macromolecule to form a solid surface-protein-second macromolecule complex followed by disruption of the solid surface-protein bond as described in step d) of instant claim 1. See Yu et al: col. 19, lines 9-37; col. 15, lines 4-13; col. 13, lines 52-57; col. 12, line 43 – col. 13, line 5. The method of Yu et al anticipates the method of instant claim 1. Note that instant claim 1 does not require any specific type of "stable bond between the solid-surface and the protein conjugate".

7) Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al (U.S. 6,492,105 B2).

Yu et al is applied for the reasons stated in the above rejection of claim 1 under 35 USC 102(e).

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Although Yu et al describes the production of protein-protein conjugates by the method outlined above, Yu et al does not specifically describe the use of an antibody, a well known type of protein, in the preparation of an antibody-protein conjugate as recited in instant claim 19. However, given the fact that an antibody is a well known protein (polypeptide), it would be obvious to substitute an antibody as an equivalent protein reactant in the method of Yu et al with the expectation of obtaining a similar, equivalent soluble or suspended protein-antibody conjugate, as claimed.

8) Claims 1, 19 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Schwartz (U.S. 2003/0013857 A1).

Schwartz describes a method of attaching a protein to a functionalized solid surface through a hydrazone linkage to form a solid surface-protein complex as described in steps a) through c) of instant claim 1 wherein hydrazide-containing macromolecules were immobilized to a functionalized solid support via hydrazone bond formation. The solid surface-protein complex of Schwartz is then further contacted with a second macromolecule to form a solid surface-protein-second macromolecule complex followed by disruption of the solid surface-protein bond as described in step d) of instant claim 1 to form a biomolecule-biomolecule conjugate. See Schwartz: paragraphs [0110] – [0112], [0018], [0147], [0172], [0175] - [0181] and EXAMPLE 17. For the use of an antibody “biomolecule” as a component of the soluble conjugate (instant claims 19 and 20), see Schwartz, paragraph [0180].

9) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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10) Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Merrifield (reference AK of form PTO-1449).

Merrifield describes the reaction of an amino acid with a solid phase support to form an amino acid-solid phase complex. This complex is then further reacted with additional amino acids (forming a peptide) to attach these additional biomolecules to the support via reaction of a functional group on the amino acid first attached to the solid support. The resulting amino acid conjugate attached to the solid support is then cleaved from the support. Merrifield uses single amino acids as reactants rather than proteins (polypeptides comprised of amino acids) as in the instantly claimed method. See Merrifield: page 2149, the second paragraph of the first column; Fig. 1; page 2153, The Peptide Liberation Step. The combination of steps described in Merrifield involves the same chemistry as required by the method steps of instant claim 1, i.e. forming a stable disruptable bond between a surface and an amino acid, reacting the attached amino acid with another amino acid and finally disrupting the bond between the first amino acid and the solid support. {Note that instant claim 1 does not require the formation of any specific types of chemical bonds in any step.}

Given the fact that the Merrifield method involves the same set of reactions of amino acid components, *amino acids being the same reactive components of the proteins (polypeptides) used in the instantly claimed method*, it would be well within the skill of the art and therefore obvious to substitute proteins for amino acids as reactants in the method of Merrifield, as claimed, with the expectation of obtaining a similarly useful method for forming soluble protein-protein conjugates.

11) The following references are cited to further show the state of the art.

Thorpe (U.S. 5,762,918): col. 19, lines 52-67; King et al: Biochemistry (1986), vol. 25, pp. 5774-5779; Healy et al (US 2004/0001892 A1: Fig. 1 and paragraphs [0174] – [0176].


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12) An inquiry of a general nature which is **not related to the prosecution on the merits** should be directed to Technology Center 1600 telephone number (571) 272-1600. The general fax number for the USPTO is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823.

July 23, 2004


Mary (Molly) E. Ceperley
Primary Examiner
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